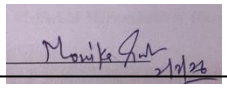
CERTIFICATE BY GUIDE

Certified that **DR. DIKSHITA DEKA,** is a Bonafede post-graduate student in the department of Oral and Maxillofacial Surgery in M. M. College of Dental Sciences and Research, Mullana, District Ambala, Haryana and is registered with M. M. (Deemed to be) University, Mullana, Ambala. She shall carry out genuine, scientific research work on her dissertation project on **"Comparative analysis of Hyaluronic acid gel vs A-PRF in extraction socket among smokers"** under our direct supervision.



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INTRODUCTION

Post-extraction socket healing is a fundamental process in dentistry, as it directly determines the predictability and its long-term success for any prosthetic rehabilitation. Healing of the extraction socket involves a coordinated sequence of biological events—coagulation, inflammation, tissue proliferation, and remodeling. That works together to repair and support the development of functional and aesthetic tissues. [1]

Various factors like oxygenation, infection, age, sex hormones, stress, medications, obesity, smoking and nutrition affect wound healing. [2] In developed countries, where at least 25% of adults smokes cigarettes, tobacco use constitutes the most significant preventable cause of morbidity and premature mortality. [3] Smoking is associated with several complications after extraction, including delayed wound (soft tissue and hard tissue) healing and sometimes development of dry socket. Cigarette smoking impairs bone repair via multiple biological pathways. Nicotine and other tobacco components induce vasoconstriction in small blood vessels, limiting oxygen and nutrient delivery to the injury site and thereby delaying bone healing. Smoking further inhibits angiogenesis, which is essential for early bone repair. Tobacco reduces intestinal calcium absorption—a critical mineral for bone formation—resulting in structurally weaker bone and also disrupts hormonal regulation of bone metabolism, fostering a

catabolic state. Additionally, cigarette smoke hinders the conversion of mesenchymal stem cells into osteoblasts, which impair the functionality of bone marrow to regenerate bone at socket site. [4] Numerous studies have demonstrated that smoking delays wound healing and adversely affects bone remodeling which can disrupt the biological events and negatively impact the success of subsequent dental treatments. [5] Tobacco acts as a peripheral vasoconstrictor, and its constituents, such as nicotine, increases platelet adhesiveness, elevate the risk of microvascular occlusion, and lead to tissue ischemia. Additionally, smoking stimulates the release of catecholamines, leading to vasoconstriction and reduced tissue perfusion. [6] CO produced during the combustion of tobacco diminishes oxygen transport and metabolism, whereas Hydrogen Cyanide produced during smoking inhibits the enzyme systems necessary for oxidative metabolism and oxygen transport at the cellular level leading to slower wound healing in smokers. [7]

Advanced platelet-rich fibrin (A-PRF) is prepared using patient's own blood sample, which is centrifuged at a specific speed of 1500 rpm for 14 minutes, unlike the conventional platelet-rich fibrin which is produced at 3000 rpm for 10 minutes. Shahram Ghanaati highlighted that reducing the centrifugation speed and extending the duration in A-PRF preparation results in a greater concentration of platelets and neutrophilic granulocytes in the distal portion of the clot. The increased presence of cells (platelets and neutrophilic granulocytes) affect the differentiation of both host macrophages and those within the clot, potentially enhancing bone and soft tissue

regeneration. [8]

Hyaluronic acid is a naturally occurring polysaccharide found in the connective tissues of vertebrates. It is a high–molecular-weight glycosaminoglycan composed of repeating units of glucuronic acid and N-acetylglucosamine. [9] Extensive research has demonstrated that hyaluronic acid (HA) is highly effective in wound healing by stimulating granulation tissue formation, reducing inflammation, and promoting both re-epithelialization and angiogenesis. [10] Hyaluronic acid also plays a vital role in bone regeneration by enhancing the proliferation, adhesion, and migration of undifferentiated mesenchymal cells and promoting their differentiation into osteoblastic cells. [12] Hyaluronic acid is also non-immunogenic and non-toxic, making it a safe material used in a wide range of medical applications. [13]

Currently there is no evidence directly comparing the beneficial effects of A-PRF and hyaluronic acid gel on socket healing in smokers. That’s why, this prospective current study design has been hatched, which aims to assess and compare the effect of A-PRF vs Hyaluronic Acid gel on healing of extraction socket among smokers.

AIM AND OBJECTIVES

AIM:

To compare the efficacy of Hyaluronic Acid gel vs A-PRF in the healing of extraction socket among smokers.

OBJECTIVES:

- To monitor the post-operative pain using **Wong Baker scale**.
- To monitor the post-operative discomfort using Postoperative Symptom Severity Scale **(PoSSe Scale)**.
- To monitor post-operative wound healing using **Southampton scoring** system.
- To record radiological changes in bone healing for both quality and quantity of bone regeneration by evaluating bone density, trabecular pattern and bone height using Bone healing index by **Kelly et al**.
- To assess any other complications that may arise.

REVIEW OF LITERATURE

- **Ceylan Şen et al**. (2025) conducted a randomized, examiner-masked clinical trial to assess the impact of hyaluronic acid (HA) and injectable platelet-rich fibrin (I-PRF) on the healing of the palatal donor site after free gingival grafting (FGG). Sixty-seven patients were randomly divided into three groups: 0.8% HA gel-impregnated gelatin sponge, I-PRF-impregnated sponge, and sterile sponge (control). The intensity of postoperative pain and burning sensation was measured using a Visual Analog Scale (VAS) on days 3, 7, 14, and 21. Complete epithelization (CE), Landry Wound Healing Index (WHI), and color match (CM) were measured at varying postoperative times. Palatal tissue thickness and oral health-related quality of life (OHRQoL) were also measured. Both HA and I-PRF reduced postoperative discomfort and improved complete epithelization compared to the control group ($p < 0.05$). HA was more effective in wound healing and morbidity than I-PRF. There was a significant difference in palatal tissue thickness at 1 and 3 months ($p = 0.001$). OHRQoL scores improved significantly between day 7 and day 14 in all groups. The study concluded that the addition of HA or I-PRF to the treatment regimen improved palatal wound healing, with HA being more effective.

- **Elkady at al.** (2025) investigated the effectiveness of locally applied platelet-rich fibrin (PRF) and 0.8% hyaluronic acid (HA) in minimizing postoperative complications after the surgical removal of impacted mandibular third molars. The study comprised 66 healthy patients aged 19-29 years with partially erupted lower third molars. All surgeries were carried out under local anesthesia, and patients were randomly divided into three groups: PRF applied locally to the extraction socket, 0.8% HA (Gengigel®) applied locally, and a control group with no additional material. The postoperative pain, swelling, and trismus were evaluated on the 1st, 3rd, and 7th postoperative days. The findings revealed that 0.8% hyaluronic acid significantly alleviated pain and swelling on the 1st and 3rd postoperative days compared to the control group. The PRF group showed significantly reduced pain on the 1st day and decreased swelling on the 3rd day compared to the control group. However, there were no statistically significant differences among the groups regarding trismus. The authors concluded that both HA and PRF were effective in minimizing

postoperative pain and swelling following third molar surgery, with hyaluronic acid showing relatively better results.

- **Kokash et al**. (2023) carried out a split-mouth randomized controlled trial to assess whether combining hyaluronic acid with collagen helps minimize postoperative swelling and trismus after surgically removing impacted lower third molars. They enrolled 20 patients, each with matching bilateral impactions, for a total of 40 sites. In every case, one socket got plain collagen, while the opposite side received collagen plus hyaluronic acid for a direct side-by-side comparison within the same person. Mouth opening (for trismus) and facial swelling were measured on days 3 and 7 after surgery. The hyaluronic acid–collagen combo led to less trismus than collagen alone on both days, with no statistical significance on day 3 but a clear advantage for the combo group on day 7. Swelling was notably lower in the hyaluronic acid group on both days overall, except for one specific facial measurement on day 3. The researchers wrapped up by stating that adding hyaluronic acid to collagen effectively cuts down on post-op swelling and trismus in these procedures, suggesting it could be a valuable add-on in everyday oral surgery to ease recovery and manage inflammation for better healing.

- **Al-Saadi and Al-Quisi** (2023) conducted to assess the efficacy of advanced platelet-rich fibrin (A-PRF) and 1% hyaluronic acid (HA) gel in facilitating early soft tissue healing following the surgical extraction of impacted mandibular third molars. The study was performed in an oral surgery unit, and patients were randomly assigned into three groups. In the control group, the extraction socket received no additional material. In the HA group, 1 cc of 1% hyaluronic acid gel with a gel foam sponge was placed intra-orally. In the A-PRF group, an A-PRF clot was placed in the surgical site. Soft tissue healing was evaluated at 24 hours and on the 3rd and 7th postoperative days. Both HA and A-PRF groups showed significantly better early soft tissue healing than the control group. The A-PRF group showed statistically superior healing than the HA group on the 1st and 3rd postoperative days. However, on the 7th postoperative day, there was no statistically significant difference between the two test groups. The study concluded that both 1% hyaluronic acid gel and A-PRF are effective in facilitating early soft tissue healing after third molar surgery, and hyaluronic acid gel is an easily accessible alternative to A-PRF.

- **Shuborna et al.** (2022) conducted a split-mouth clinical trial to assess the efficacy of intra-socket hyaluronic acid (HA) in minimizing postoperative complications after bilateral mandibular third molar extractions. Thirty patients undergoing bilateral lower wisdom tooth extraction were selected. In the study sites, 0.7 ml of 20 mg/2 ml HA solution (Hyalgun) was placed intra-socket using gel foam as a carrier, while gel foam alone was used in the control sites. Postoperative swelling was measured by five facial landmarks, and maximum mouth opening was measured preoperatively and on the 2nd and 7th postoperative days. Pain intensity was measured by Visual Analog Scale (VAS) on the 1st, 2nd, and 3rd postoperative days. Analgesic intake was also measured for seven days postoperatively. The findings revealed that the HA group had significantly less swelling, trismus, and analgesic intake on the 2nd and 7th postoperative days than the control group. Moreover, VAS pain scores on postoperative days 1, 2, and 3 were significantly lower in the HA-treated sites ($p = 0.05$). The study concluded that the intra-socket use of hyaluronic acid is effective in minimizing postoperative pain, swelling, and trismus following lower third molar surgery, thus enhancing patient comfort and ease of recovery.

- **Marouf at al.** (2021) investigated the effectiveness of locally applied platelet-rich fibrin (PRF) and 0.8% hyaluronic acid (HA) in minimizing postoperative complications after the surgical removal of impacted mandibular third molars. The study comprised 66 healthy patients aged 19-29 years with partially erupted lower third molars. All surgeries were carried out under local anesthesia, and patients were randomly divided into three groups: PRF applied locally to the extraction socket, 0.8% HA (Gengigel®) applied locally, and a control group with no additional material. The postoperative pain, swelling, and trismus were evaluated on the 1st, 3rd, and 7th postoperative days. The findings revealed that 0.8% hyaluronic acid significantly alleviated pain and swelling on the 1st and 3rd postoperative days compared to the control group. The PRF group showed significantly reduced pain on the 1st day and decreased swelling on the 3rd day compared to the control group. However, there were no statistically significant differences among the groups regarding trismus. The authors concluded that both HA and PRF were effective in minimizing postoperative pain and swelling following third molar surgery, with hyaluronic acid showing relatively better results.

- **Frenkel's at al.** (2014) reviewed the biological role of hyaluronan (HA) in wound healing and its clinical applications in wound management. Hyaluronan, also known as hyaluronic acid or hyaluronate, is a polymorphic glycosaminoglycan that is widely distributed in the body, with a high affinity for the skin. Due to its hygroscopic properties and viscoelasticity, HA has a crucial role in maintaining tissue hydration, integrity, and extracellular matrix homeostasis. The author discussed the role of HA in all stages of normal wound healing. During the inflammatory stage, HA is involved in cell migration and the regulation of inflammation. During the proliferative stage, HA is involved in fibroblast proliferation, angiogenesis, and granulation tissue formation. During the remodeling stage, HA is involved in extracellular matrix stabilization and tissue maturation. The review also discussed the clinical application of HA-based wound dressings, with a focus on their biocompatibility, ability to maintain a moist wound environment, and potential to enhance tissue repair. The author concluded that hyaluronan is a major regulator of wound healing and a valuable therapeutic agent in clinical wound care management.

- **Balaji's at. al** (2008) reviewed how smoking tobacco impedes healing after surgery in the oral cavity, as it negatively affects the healing process in oral and maxillofacial surgery. It also explains how smoking negatively affects the healing process after tooth extraction (surgical or not), general maxillofacial surgery, dental implants, and periodontal procedures. Laboratory evidence shows that it inhibits bone growth, such as in distraction osteogenesis procedures. The major contributing factors include the vasoconstrictor properties of tobacco, as nicotine increases platelet stickiness, causes micro vessel occlusion, results in tissue ischemia, and leads to catecholamine release for further vasoconstriction. Smoking also compromises the body's natural immunity, particularly affecting neutrophils, thereby increasing the risk of infection and impairing healing. The author concluded that smoking always delays healing after oral surgery; therefore, advising patients to stop is essential.

MATERIALS AND METHODS

STUDY DESIGN:

This study will include 200 smoker patients for comparing the efficacy of Hyaluronic Acid gel vs A-PRF placed in extraction socket of premolars and molars of both the jaws.

STUDYSETTING:

This clinical study will be carried out on 200 smoker patients who will be requiring non-surgical extraction of premolars and molars of both the jaws. Once the Institutional Research Review Board and Institutional Ethical Committee will give their proper clearance, the study will be proceeded.

SOURCE OF DATA:

The study will include 200 smoker patients reporting to the OPD (outpatient department) of the Department of Oral and Maxillofacial Surgery at Maharishi Markandeshwar College of Dental Sciences & Research (MMCDSR), Mullana, Ambala, for the extraction of premolars and molars of both the jaws and who will be willing to participate in the study after obtaining informed consent.

SELECTION CRITERIA:

INCLUSION CRITERIA:

- Patients above 18 years and below 60 years of age.
- Patient requiring premolar and molar extraction.
- Atraumatic extractions.

- Patient habituated to smoking (tobacco products).
- Patient in ASA-I and ASA-II category.
- Operative site should be free of active infection.
- Patient should be co-operative.
- The patient should be willing to participate in the study.

EXCLUSION CRITERIA:

- Age below 18 years.
- Patients with impaired bone metabolism.
- Patient undergoing surgical extraction.
- Patients who are allergic to the local anaesthetic solution.
- Patients taking drugs that might interfere with healing.
- Patients having systemic disorders which may interfere with healing.
- Patients who give history of having or are undergoing any radiation/chemotherapy to the head and neck region.

STUDY MATERIAL:

- Hyaluronic Acid Gel (0.3% w/v)
- A-PRF

SAMPLE SIZE:

200 smokers requiring extraction of premolars and molars of both the jaws.

SELECTION OF GROUP:

200 patient's slips will be divided randomly by Envelope method. An equal number of allocation slips for Group A (Hayluronic Acid gel) and Group B (A-PRF) will be made, folded, and put in

an identical opaque sealed box. The envelopes will be well mixed and groups will be allocated during the procedure.

PARAMETERS TO BE STUDIED:

1. Pain
2. Discomfort
3. Wound healing
4. Bone healing
5. Any other complications arising

ARMAMENTARIUM:

- Probes
- Mouth mirrors
- Tweezers
- Disposable syringes (2ml) with needles (24 gauge)
- Lox 2%. (Lignocaine 2% with adrenaline 1:2,00,000)
- Molt's #9 Periosteal elevators
- Adson's tissue holding forceps- Toothed and non-toothed
- Coupland elevators
- Warwick James elevators
- Cryer elevators
- Molar extraction forceps
- Luca's curette
- Suction tips
- Suction tube
- Sterile gauze
- Bone rongeurs

- Bone files
- Needle holders
- Scissors
- 3-0 silk reverse cutting suture
- Suture cutting scissors

PREOPERATIVE PROCEDURE:

A detailed case history will be taken from all the participants before the surgical procedure. This will include demographic information, medical, dental, drug and personal history. Special attention will be given to personal history with regards to smoking or tobacco consumption. Patient will be advised for preoperative IOPA Radiograph of the tooth to be extracted. Prior to the extraction, the patient will be asked to rinse mouth with 0.2% chlorhexidine for 30 seconds.

PREPARATION OF A-PRF:

Prior to giving anaesthesia, a tube of 10 ml venous blood will be collected from patient in glass coated plastic tube and immediately centrifuged at 1500 rpm for 14 min. The blood sample separates into three distinct layers:

1. An acellular plasma layer at the top, with no cellular material.

2. A polymerized fibrin clot in the middle, containing a dense 3D matrix. It has higher concentration of platelets, growth factors (such as PDGF, TGF-β1, VEGF), and white blood cells (leukocytes).

3. A lower layer consisting of concentrated blood cells (red corpuscle base) at the bottom of the test tube.

The middle layer (PRF clot) will be removed using sterile tweezers and separated by scissors from the underlying red corpuscular base.

PREPARATION OF HYALURONIC ACID GEL:

A sterile 0.3% hyaluronic acid gel (GingiCare) will be dispensed from its original tube into a 2-ml disposable syringe under aseptic conditions. Then, the gel will be uniformly poured onto an

ABGel absorbable Gelatine foam until complete saturation will be achieved. The prepared HA-impregnated ABGel will be immediately placed into the extraction socket following premolar and molar extraction.

SURGICAL PROCEDURE:

- All surgical procedure will be performed under aseptic condition in accordance with set surgical protocols.
- Lignocaine Hydrochloride with 1:2,00,000 epinephrine will be administered.
- Gingiva will be separated using periosteal elevator.
- Appropriate premolar or molar forcep will be engaged following adequate placing.
- Controlled bucco-lingual and rotational movements will be applied to expand the alveolar socket and facilitate tooth removal.
- Curettage of the extraction sites will be done with curette and smoothening of the sharp bony margins of socket will be done with bone file.
- A-PRF will be placed using a sterile tweezer in extraction socket of Group A and ABGel soaked with Hyaluronic Acid gel in Group B.
- Closure of extraction socket will be achieved with simple interrupted sutures using 3-0 silk sutures.
- Post-operative instructions will be given to all patients.
- Post extraction medications that will be prescribed:

1. Capsule Amoxicillin 500mg 3 times a day for 5 days.
2. Tablet Metronidazole 400mg 3times a day for 5 days.
3. Tablet Diclofenac sodium 3times a day for 3 days

- After the extraction, patients will be followed up on 3rd day, 7th day, 3rd month and 6th month postoperatively for the evaluation of the parameters.

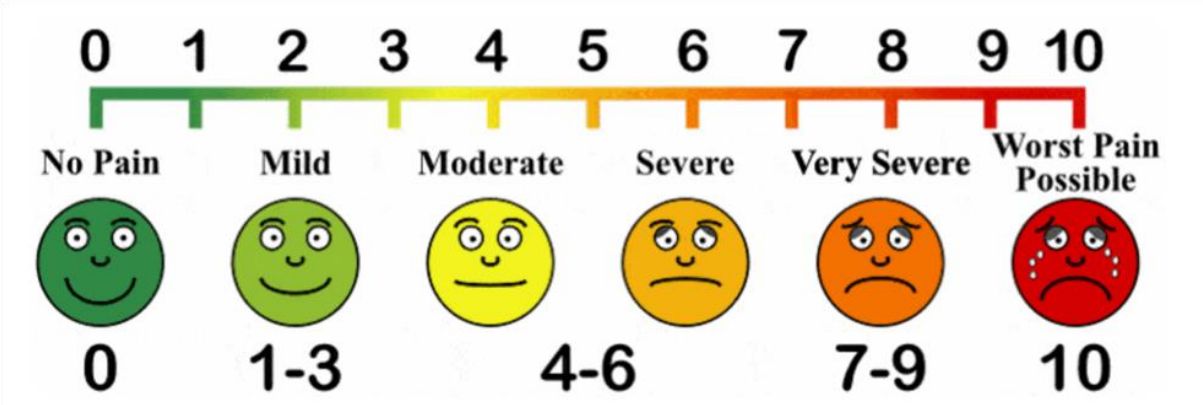
POST OPERATIVE EVALUATION PARAMETERS

Both the groups will be evaluated on the following clinical parameters:

- **PAIN -**The estimation of pain will be done subjectively,

❖ by recording verbal response of the patient;

❖ to rate his/her nociceptive experience on **Wong Baker scale** [11] which ranges from 0-10.



The values will be recorded postoperatively at 3rd day and 7th day respectively.

- **DISCOMFORT** - The estimation of discomfort will be done subjectively,

❖ by recording verbal response of the patient to the questionnaire using Postoperative Symptom Severity Scale **(PoSSe Scale)** [13];

❖ The PoSSe scale assesses patient-perceived adverse effects in 7 areas: eating, speech, sensation, appearance, pain, sickness, and daily activities. A score was assigned to the possible responses to each forced question. The scores of the responses to each question were summed.

❖ To rate his/her experience on **Visual Analog scale** [14] which ranges from 0-10

The values will be recorded postoperatively (on 3rd day and the 7th day).

- **PRIMARY WOUND HEALING -**will be evaluated on the 3rd and 7th day post operatively with photographs of the extraction site and will be graded accordingly.
- Different grades of wound healing according to **Southampton scoring** system [15]

Grading	APPEARANCE
0	Normal healing
I	Normal healing with mild bruising or erythema
II	Erythema plus other signs of inflammation
III	Clear or haemoserous discharge
IV	Major complication Pus Discharge
V	Deep or severe wound infection with or without tissue break Down; haematoma

- **RADIOLOGICAL FOLLOWUP PARAMETER –** will be evaluated postoperative 3rd and 6th month with IOPA Radiograph of the socket site.

- ❖ Bone height will be measured radiologically at a distance between inferior most part of the socket till highest point of the alveolar bone height achieved after the placement on 3rd month, 6th month using IOPA Radiograph.
- ❖ Alveolar bone density of regenerate will be measured radiographically at the region of molar socket, immediately after extraction, 3rd month, 6th month using ImageJ software, NIH, USA on digital IOPA Radiograph.
- ❖ Bone healing assessment will be done using Bone healing Index given by Kelly et al.
- ❖ This method grades two parameters on a 5-point scale (-2 to +2), namely, Overall density and Trabecular pattern (Kelly et al., 1980).
- ❖ The baseline preoperative radiograph is given a score of 0; a score of -1 to +1 indicates moderate deviation from normal, while a score of -2 to +2 indicates significant deviation.

GRADE	**Overall Density**
+2	Severe increase in radiographic density

+1	Mild to moderate increase in radiographic density
0	Within normal limits
-1	Mild to moderate decrease in radiographic density
-2	Severe decrease in radiographic density
GRADE	**TRABECULAR PATTERN**
+2	All trabeculae substantially coarser
+1	Some coarser trabeculae; milder degrees
0	Within normal limits
-1	Delicate finely meshed trabeculations
-2	Granular, nearly homogenous patterns; individual trabeculations essentially absent

CLINICAL SIGNIFICANCE

The use of local biological agents like Hyaluronic acid and A-PRF has been suggested to improve both soft and hard tissue healing of extraction sockets by counteracting the harmful effects of smoking like delayed wound healing and sometimes dry socket. This study compares the efficacy of Hyaluronic Acid and A-PRF in reducing pain, swelling, post-operative discomfort, and in enhancing soft tissue wound healing and bone healing following premolar and molar extraction in smokers. The results can aid clinicians in selecting appropriate adjunct during routine oral surgical practice involving compromised patients.

Conflict of interest: None

Sponsorship: Self

Copyright infringement: None

Risk of subjects: None

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PATIENT INFORMED CONSENT FORM

Title of the project: "**Comparative analysis of Hyaluronic acid gel vs A-PRF in extraction socket among smokers**.

I have been informed of the purpose of the procedure and how it will benefit my treatment. The procedure has been described to me and I understand how it will be accomplished. The nature, objective, duration and expected effects of the study have been explained to me in a language in which I am conversant. I had the time and opportunity to enquire about the studyand I have been fully satisfied with the explanations given.

•I am ready to participate voluntarily in this study.

•I understand that I am at liberty to withdraw from this study at any time without justifyingmy decision to withdraw.

- I know that the results from this study may be forwarded to the suitable authorities,presented in scientific meetings and published.
- By signing this consent form, I have not given up any legal rights which I am otherwiseentitled to as subject in this study.

•I know that I will be given a copy of this consent form which is signed and dated.

Signature of the participant:_____Date:

Signature of the witness:_____Date:

Signature of the investigator:_____Date:

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